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EXAMINER	
DINNER D	
ART UNIT	**PAPER NUMBER**
129	6

DATE MAILED: 05/02/85

This is a communication from the examiner in charge of your application.

COMMISSIONER OF PATENTS AND TRADEMARKS

5/2/85

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~_____ days~~ from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449
4. ☐ Notice of informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-23 are pending in the application.
   Of the above, claims 21-23 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-20 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.
8. ☐ Allowable subject matter having been indicated, formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. These drawings are ☐ acceptable; ☐ not acceptable (see explanation).
10. ☐ The ☐ proposed drawing correction and/or the ☐ proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved. ☐ disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections MUST be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.
12. ☒ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☒ been received ☐ not been received
    ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

PTOL-326 (Rev. 7 - 82) **EXAMINER'S ACTION**

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-20 are, drawn to 4-membered lactone compounds, classified in Class 549, subclass 263.

II. Claims 21-23 are, drawn to method of use in commercially produced food stuffs, classified in Class 426, subclass 531.

The inventions are separate and distinct, each from the other because of the following reasons:

Inventions Group I and Group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product(MPEP 806.05(h)). In the instant case the product as claimed can be used in a materially different process such as pharmaceutical usage, which also has the therapeutic composition included in that class/subclass (514/449).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter restriction for examination purposes as indicated is proper.

During a telephone conversation with Mr. Johnson on

4/18/85 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-20. Affirmation of this election must be made by applicant in responding to this Office action.

Claims 21-23 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an enabling disclosure. This paragraph of the statute requires that the specification shall contain a written description of the invention and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

MPEP 608.01(p) sets forth 3 requirements for deposition of microorganisms. Applicant has not provided assurance of permanent availability (sub-paragraph 3.) Permanence is generally deemed to be 30 years or more.

The specification is also non-enabling for "commercially-produced foodstuff." No dosage ranges/formulations or utility is ~~shown~~ seen for the compounds disclosed herein in combination with "foodstuffs".

No enablement is seen for the treatment of obesity in mammals. Reduction of triglycerides is not, to Examiners knowledge, correlated with reduction of fat cells in mammals. Information on such is requested if this is the mode of action perceived.

Table I, column 3 page 6-LD50 for tetrahydro lipstatin; it is unclear if the hypene refers to no toxicity or whether it is 100% toxic in oral form.

The designation on pll for fermentors (line 16): Should there be a hypen or semicolon between such numbers? Same problem in example 1 p.15, line 22; p. 16 lines 18, 22, 25 etc.

P. 11 dealing with preferred salts for additives in culture medium. Are heavy metal and various other metal salts included and if so in what quantities for detrimental effects?

No enablement is seen for maximal production and accumulation times of the claimed compound in the cultivation stage.

Typo error on p.12 line 36- "perinterally".

The specification is not enabling for "control and prevention of illness". Is applicant contemplating hirsutism for instance?

Example 1, incubation under aerobic conditions, is this including submerged aerobic conditions?

Claims 1-20 are rejected under 35 U.S.C. 112, first

paragraph, for the reasons set forth in the objection to the specification.

Claims 4-8 are rejected under 35 U.S.C. 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"No effective amount" of compound is seen in claim 4. 5-95% of the formula weight of the composition can be an ineffective amount. It is suggested that such term be incorporated into claim 4.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-20 are rejected under 35 U.S.C. 103 as being unpatentable over Umezawa et al (4,189,438 and 4,202,824 4,358,602).

Umezawa et al teach structurally similiar compounds to have pharmaceutical use, in particular, activity against cholesterol. (PN 4202824); see abstract and col. 1, line 20-24 which teaches activity of such compounds to have enzymatic inhibition against a large number of enzymes. (Broadly included in this is would be applicants enzyme pancreas lipose). Also taught is the use of ebelactones, (still structurally similiar) to have imuno-activity ~~when~~ like the esterastin compounds above. Notable here is that absence of the ester linked chain (containing the amide functional group), a modification of the same portion which applicant also changes still produces the same utility. It would therefore be expected that applicants compounds would have the same use therein, Umezawa et al (PN ~~4358602~~ 4242453) is cited to show state of the art for micro-organism cultivation. Applicant is requested to include in the Abstract production of said compounds by the cultivation of microorganism Steptomyces toxytricini identified as NRRL 15443.

Applicant is also requested to consider a title change to something more informative of the type of compounds. A possible suggestion is "physiologically

active carbamoyl derivatives of esterastin".

No claim is allowed.

Please direct all communication concerning this application to Ms. Dinner.

Dinner:wcg

A/C 703

557-3920

4/26/85

GLENNON H. HOLLRAH
SUPERVISORY PATENT EXAMINER
ART UNIT 129